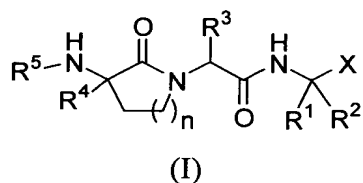


WHAT IS CLAIMED:

1. A method for treating cancer comprising administering to a mammal in need thereof, either alone or in combination with at least one other anticancer agent, a therapeutically effective amount of a compound of Formula I:



- 10 or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein

the lactam ring of Formula (I) is substituted with 0-2 R^b;

X is selected from the group:

- 15 B(OH)₂, BY¹Y², and C(=O)C(=O)NHR^{1a};

Y¹ and Y² are independently selected from:

- a) -OH,
 b) -F,
 20 c) -NR¹⁸R¹⁹,
 d) C₁-C₈ alkoxy, or

when taken together, Y¹ and Y² form:

- e) a cyclic boron ester comprising from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;
 25 f) a cyclic boron amide comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O; or
 g) a cyclic boron amide-ester comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

- 30 R¹ is selected from the group:

C₁₋₁₀ alkyl substituted with 0-3 R^a;
C₂₋₁₀ alkenyl substituted with 0-3 R^a;
C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
C₃₋₆ cycloalkyl substituted with 0-3 R^a;

5

R^{1a} is selected from the group:

C₁₋₁₀ alkyl substituted with 0-3 R^a;
C₂₋₁₀ alkenyl substituted with 0-3 R^a;
C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
C₃₋₆ cycloalkyl substituted with 0-3 R^a;

10

R^a is selected at each occurrence from the group:

C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH, -S-
C₁₋₆ alkyl;

15

phenyl substituted with 0-3 R^b;
naphthyl substituted with 0-3 R^b;
-O-(CH₂)_q-phenyl substituted with 0-3 R^b;
-O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:

20

O, S, and N, and substituted with 0-3 R^b;

R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,
OCF₃, and C₃₋₆ cycloalkyl;

25

R² is H;

alternatively, R¹ and R² combine to form a C₃₋₅ cycloalkyl group;

30

R³ is selected from the group:

- C₁₋₆ alkyl substituted with 0-2 R^a;
- C₂₋₆ alkenyl substituted with 0-2 R^a;
- C₂₋₆ alkynyl substituted with 0-2 R^a;
- 5 -(CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;
- (CH₂)_q-phenyl substituted with 0-2 R^a;
- (CH₂)_q-naphthyl substituted with 0-2 R^a; and
- (CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4
 heteroatoms selected from the group:
- 10 O, S, and N, and substituted with 0-2 R^a;

R⁴ is selected from the group:

- H;
- C₁₋₆ alkyl substituted with 0-3 R^b;
- 15 phenyl substituted with 0-3 R^b;
- benzyl substituted with 0-3 R^b; and
- phenethyl substituted with 0-3 R^b;

R⁵ is H or Q-R^{5a};

20

Q is 0, 1, 2, or 3 amino acids;

R^{5a} is selected from the group:

- S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆
- 25 alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

- C₁₋₆ alkyl substituted with 0-3 R^c;
- phenyl substituted with 0-3 R^c;
- 30 naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:

O, S, and N, substituted with 0-3 R^c;

5

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and

10

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:

O, S, and N, substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

15

C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,

NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

H and CH₃;

20

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

R⁸ is selected from the group:

25

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

R¹⁸ and R¹⁹ at each occurrence are independently selected from H, C₁₋₄ alkyl,
aryl(C₁₋₄ alkyl)-, and C₃₋₇ cycloalkyl;

30 n is selected from the group:

1, 2, and 3; and

q is selected the group:

0, 1, and 2.

5 2. The method according to claim 1 wherein:

Y¹ and Y² are independently selected from:

a) -OH,

b) C₁-C₈ alkoxy, or

10 when taken together, Y¹ and Y² form:

c) a cyclic boron ester comprising from 2 to 20 carbon atoms;

R¹ is selected from the group:

C₁₋₆ alkyl substituted with 0-3 halogen; and

15 C₂₋₆ alkenyl substituted with 0-3 halogen;

R^a is selected at each occurrence from the group:

C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH, -S-C₁₋₆ alkyl;

20 phenyl substituted with 0-3 R^b;

naphthyl substituted with 0-3 R^b;

-O-(CH₂)_q-phenyl substituted with 0-3 R^b;

-O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms

25 selected from the group:

O, S, and N, and substituted with 0-3 R^b;

R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,

30 OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

R³ is selected from the group:

- C₁₋₆ alkyl substituted with 0-2 R^a;
- 5 C₂₋₆ alkenyl substituted with 0-2 R^a;
- C₂₋₆ alkynyl substituted with 0-2 R^a;
- (CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;
- (CH₂)_q-phenyl substituted with 0-2 R^a;
- (CH₂)_q-naphthyl substituted with 0-2 R^a; and
- 10 -(CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4
heteroatoms selected from the group:
O, S, and N, and substituted with 0-2 R^a;

R⁴ is selected from the group:

- 15 H;
- C₁₋₆ alkyl substituted with 0-3 R^b;
- phenyl substituted with 0-3 R^b;
- benzyl substituted with 0-3 R^b; and
- phenethyl substituted with 0-3 R^b;

20

R⁵ is H or Q-R^{5a};

Q is 0, 1, 2, or 3 amino acids;

25 R^{5a} is selected from the group:

- S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆
alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

- 30 C₁₋₆ alkyl substituted with 0-3 R^c;

phenyl substituted with 0-3 R^c;
 naphthyl substituted with 0-3 R^c;
 benzyl substituted with 0-3 R^c; and
 5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
 5 selected from the group:
 O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:
 phenyl substituted with 0-3 R^c;
 10 naphthyl substituted with 0-3 R^c;
 benzyl substituted with 0-3 R^c; and
 5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
 selected from the group:
 O, S, and N, substituted with 0-3 R^c;

15
 R^c is selected at each occurrence from the group:
 C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,
 NR^dR^d, -CN, and NO₂;

20 R^d is selected at each occurrence from the group:
 H and CH₃;

R⁷ is selected at each occurrence from the group:
 H and C₁₋₆ alkyl;

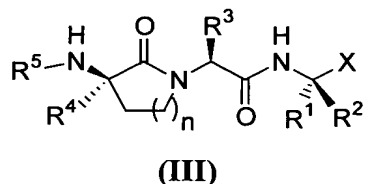
25
 R⁸ is selected from the group:
 C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

n is selected from the group:
 30 1, 2, and 3; and

q is selected from the group:

0, 1, and 2.

3. A method for treating cancer comprising administering to a mammal in need thereof, either alone or in combination with at least one other anticancer agent, compound having Formula (III):



10

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

X is a boronic acid or a boron ester of formula BY¹Y²;

- 15 Y¹ and Y² are independently selected from:

a) C₁-C₆ alkoxy, or

when taken together, Y¹ and Y² form:

b) a cyclic boron ester comprising from 2 to 16 carbon atoms;

- 20 R¹ is selected from the group:

ethyl, n-propyl, i-propyl, n-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R^a is selected at each occurrence from the group:

- 25 C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH, -S-C₁₋₆ alkyl;

phenyl substituted with 0-3 R^b;

naphthyl substituted with 0-3 R^b;

-O-(CH₂)_q-phenyl substituted with 0-3 R^b;

- 30 -O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:

O, S, and N, and substituted with 0-3 R^b;

5 R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,
OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

10

R³ is selected from the group:

C₁₋₆ alkyl substituted with 0-2 R^a;

C₂₋₆ alkenyl substituted with 0-2 R^a;

C₂₋₆ alkynyl substituted with 0-2 R^a;

15 -(CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;

-(CH₂)_q-phenyl substituted with 0-2 R^a;

-(CH₂)_q-naphthyl substituted with 0-2 R^a;

-(CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4
heteroatoms selected from the group:

20 O, S, and N, and substituted with 0-2 R^a;

R⁴ is selected from the group:

H, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl;

phenyl substituted with 0-3 R^b;

25 benzyl substituted with 0-3 R^b; and

phenethyl substituted with 0-3 R^b;

R⁵ is H or Q-R^{5a};

30 Q is 0, 1, or 2 amino acids;

R^{5a} is selected from the group:

-S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆ alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

5 R⁶ is selected from the group:

C₁₋₆ alkyl substituted with 0-3 R^c;

phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and

10 5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;

15 naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, substituted with 0-3 R^c;

20 R^c is selected at each occurrence from the group:

C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷, NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

25 H and CH₃;

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

30 R⁸ is selected from the group:

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

n is 1 or 2; and

q is selected from the group:

5 0, 1, and 2.

4. The method of claim 3 wherein:

X is a boronic acid or boron ester, wherein the ester is a diol selected from the group:

10 pinanediol, pinacol, 1,2-ethanediol, 1,3-propanediol, 1,2-propanediol, 2,3-butanediol, 1,2-diisopropylethanediol, 5,6-decanediol, and 1,2-dicyclohexylethanediol;

R¹ is selected from the group:

15 ethyl, n-propyl, i-propyl, n-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R² is H;

20 R³ is selected from the group:

 n-propyl, n-butyl, i-butyl, n-pentyl, neo-pentyl, cyclohexylmethyl, cyclopentylmethyl, phenyl, benzyl, t-butoxymethyl, benzyloxymethyl, hydroxymethyl, methoxymethyl, ethoxymethyl, propoxymethyl, and i-propoxymethyl;

25

R⁴ is selected from the group:

 methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, phenyl, benzyl, and phenethyl;

30 R⁵ is H or Q-R^{5a};

Q is 0, 1, or 2 amino acids;

R^{5a} is selected from the group:

-S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, and -CH₂-R^{6a};

5 R⁶ is selected from the group:

methyl substituted with 0-3 R^c;

ethyl substituted with 0-3 R^c;

propyl substituted with 0-3 R^c;

butyl substituted with 0-3 R^c;

10 phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and

quinolinyl substituted with 0-3 R^c;

15 R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and

quinolinyl substituted with 0-3 R^c;

20

R^c is selected at each occurrence from the group:

methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, methoxy, ethoxy,

propoxy, i-propoxy, CF₃, OCF₃, Cl, F, Br, I, OH, phenyl, C(O)OH,

NH₂, -CN, and NO₂;

25

R⁸ is methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, phenyl, and benzyl;

and

n is 1 or 2.

30

5. The method of claim 4 wherein:

X is a boronic acid or a boron ester of formula BY^1Y^2 ;

Y¹ and Y² are individually selected from C₁-C₆ alkoxy, or when taken together, Y¹
5 and Y² form a cyclic boron ester where said chain or ring contains from 2 to
14 carbon atoms;

R¹ is selected from the group:
ethyl, n-propyl, i-propyl, n-butyl, i-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-
10 difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R² is H;

R³ is selected from the group:
15 i-butyl, neo-pentyl, cyclohexylmethyl, t-butoxymethyl, benzyloxymethyl,
hydroxymethyl, benzyl and phenyl;

R⁴ is selected from the group:
ethyl, n-propyl, i-propyl, R-2-butyl, S-2-butyl, phenyl, benzyl, and phenethyl;
20

R⁵ is selected from the group:
H,
benzyl,
m-methylphenylsulfonyl,
25 m-trifluoromethylphenylsulfonyl,
p-i-propylphenylsulfonyl,
p-propylphenylsulfonyl,
p-t-butylphenylsulfonyl,
p-carboxylphenylsulfonyl,
30 4-(1,1')biphenylsulfonyl,
1-naphthylsulfonyl,
2-naphthylsulfonyl,

8-quinolinylsulfonyl,
pyrazin-2-ylcarbonyl,
n-butylsulfonyl,
N-phenylaminocarbonyl,
5 N-(p-n-butylphenyl)aminocarbonyl,
benzyloxycarbonyl,
methoxycarbonyl,
t-butyloxycarbonyl,
benzoyl,
10 methanesulfonyl,
phenylsulfonyl,
o-nitrophenylsulfonyl,
m-nitrophenylsulfonyl, and
m-aminophenylsulfonyl; and

15

n is 1 or 2.

6. The method according to claim 5 wherein:

20 X is a boronic acid or boron ester, wherein the ester is a diol selected from the group:
pinanediol, pinacol, 1,2-ethanediol, 1,3-propanediol, 1,2-propanediol, 2,3-
butanediol, 1,2-diisopropylethanediol, 5,6-decanediol, and 1,2-
dicyclohexylethanediol;

25 R¹ is selected from the group:
ethyl, n-propyl, i-propyl, n-butyl, i-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-
difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R² is H;

30

R³ is selected from the group:

i-butyl, neo-pentyl, cyclohexylmethyl, t-butoxymethyl, benzyloxymethyl, hydroxymethyl, benzyl, and phenyl;

R⁴ is selected from the group:

5 ethyl, n-propyl, i-propyl, R-2-butyl, S-2-butyl, phenyl, benzyl, and phenethyl;

R⁵ is selected from the group:

H,
benzyl,
10 m-methylphenylsulfonyl,
m-trifluoromethylphenylsulfonyl,
p-i-propylphenylsulfonyl,
p-propylphenylsulfonyl,
p-t-butylphenylsulfonyl,
15 p-carboxylphenylsulfonyl,
4-(1,1')biphenylsulfonyl,
1-naphthylsulfonyl,
2-naphthylsulfonyl,
8-quinolinylnsulfonyl,
20 pyrazin-2-ylcarbonyl,
n-butylsulfonyl,
N-phenylaminocarbonyl,
N-(p-n-butylphenyl)aminocarbonyl,
benzyloxycarbonyl,
25 methoxycarbonyl,
t-butyloxycarbonyl,
benzoyl,
methanesulfonyl,
phenylsulfonyl,
30 o-nitrophenylsulfonyl,
m-nitrophenylsulfonyl, and
m-aminophenylsulfonyl; and

n is 1 or 2.

7. The method according to claim 1 wherein said compound is selected
5 from the group consisting of:

(1*R*)-1-({(2*S*)-3-cyclohexyl-2-(3-isopropyl-3-({(2*S*)-3-methyl-2-((2-
pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-
pyrrolidiny)propanoyl}amino)-3-butenylboronic acid (+)-pinanediol ester;

10

(1*R*)-1-({(2*S*)-3-cyclohexyl-2-(3-isopropyl-3-({(2*S*)-3-methyl-2-((2-
pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-
piperidiny)propanoyl}amino)-3-butenylboronic acid (+)-pinanediol ester;

15 (1*R*)-1-({3-((methylsulfonyl)amino)-2-oxohexahydro-1*H*-azepin-1-
yl}acetyl)amino)propylboronic acid (+)-pinanediol ester;

(1*R*)-1-{{{(2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidiny)-3-
cyclohexylpropanoyl}amino}propylboronic acid (+)-pinanediol ester
20 hydrochloride;

1*R*)-1-(((2*S*)-2-{3-(((1,1'-biphenyl)-4-ylsulfonyl)amino)-3-isopropyl-2-oxo-1-
pyrrolidiny}-3-cyclohexylpropanoyl)amino)propylboronic acid (+)-
pinanediol ester;

25

(1*R*)-1-{{{(2*S*)-3-cyclohexyl-2-(3-isopropyl-2-oxo-3-{{{(4-
propylphenyl)sulfonyl}amino}-1-pyrrolidiny)propanoyl}amino}propylboronic
acid (+)-pinanediol ester;

30 (1*R*)-1-(((2*S*)-3-cyclohexyl-2-{3-isopropyl-3-((1-naphthylsulfonyl)amino)-2-oxo-1-
pyrrolidiny}propanoyl)amino)propylboronic acid (+)-pinanediol ester;

- (1*R*)-1-(((2*S*)-2-{3-((anilinocarbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino)propylboronic acid (+)-pinanediol ester;
- 5 (1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-pyrrolidinyl)propanoyl)amino}propylboronic acid (+)-pinanediol ester;
- (1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-pyrrolidinyl)propanoyl)amino}propylboronic acid
- 10 (1*R*)-1-(((3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
- (1*R*)-1-(((3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester
- 15 hydrochloride;
- (1*R*)-1-(((3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
- 20 (1*R*)-1-(((3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
- (1*R*)-1-(((2*S*)-2-(3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid (+)-pinanediol ester;
- 25 (1*R*)-1-(((2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid (+)-pinanediol ester hydrochloride;
- 30 (1*R*)-1-(((2*S*)-2-{3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}-4-methylpentanoyl)amino)propylboronic acid (+)-pinanediol ester;

- (1*R*)-1-(((2*S*)-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid (+)-pinanediol ester;
- 5 (1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-ethyl-3-(((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-pyrrolidinyl)propanoyl}amino)-3-butenylboronic acid (+)-pinanediol ester;
- 10 (1*R*)-1-(((2*S*)-2-(3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-piperidinyl)-3-cyclohexylpropanoyl)amino}propylboronic acid (+)-pinanediol ester;
- (1*R*)-1-(((3-(((tert-butoxycarbonyl)amino)-3-isopropyl-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
- 15 (1*R*)-1-(((3-amino-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid hydrochloride (+)-pinanediol ester;
- (1*R*)-1-(((3-isopropyl-3-((methoxycarbonyl)amino)-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
- 20 (1*R*)-1-(((3-(benzoylamino)-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
- 25 (1*R*)-1-(((3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;
and
- 30 (1*R*)-1-(((3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

- (1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-pyrrolidinyl)propanoyl}amino)-3-butenylboronic acid;
- 5 (1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-piperidinyl)propanoyl}amino)-3-butenylboronic acid;
- 10 (1*R*)-1-(((3-((methylsulfonyl)amino)-2-oxohexahydro-1*H*-azepin-1-yl}acetyl)amino)propylboronic acid (+)-;
- (1*R*)-1-(((2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-3-cyclohexylpropanoyl)amino}propylboronic acid;
- 15 1*R*)-1-(((2*S*)-2-{3-(((1,1'-biphenyl)-4-ylsulfonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino)propylboronic acid;
- (1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)propanoyl)amino}propylboronic acid;
- 20 acid;
- (1*R*)-1-(((2*S*)-3-cyclohexyl-2-{3-isopropyl-3-(((1-naphthylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}propanoyl)amino)propylboronic acid;
- 25 (1*R*)-1-(((2*S*)-2-{3-((anilinocarbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino)propylboronic acid;
- (1*R*)-1-(((3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid;
- 30 (1*R*)-1-(((3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-hydrochloride;

- (1*R*)-1-{{{3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}(phenyl)acetyl)amino}propylboronic acid;
- 5 (1*R*)-1-{{{(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino))-1-pyrrolidinyl}(phenyl)acetyl)amino}propylboronic acid;
- (1*R*)-1-{{{(2*S*)-2-(3-(((benzyloxy)carbonyl)amino))-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl}amino}propylboronic acid;
- 10 (1*R*)-1-{{{(2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl}amino}propylboronic acid hydrochloride;
- (1*R*)-1-(((2*S*)-2-{3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}-4-methylpentanoyl)amino)propylboronic acid;
- 15 (1*R*)-1-{{{(2*S*)-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino))-1-pyrrolidinyl)-4-methylpentanoyl}amino}propylboronic acid;
- (1*R*)-1-{{{(2*S*)-3-cyclohexyl-2-(3-ethyl-3-(((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-pyrrolidinyl)propanoyl}amino)-3-butenylboronic acid;
- 20 (1*R*)-1-{{{(2*S*)-2-(3-(((benzyloxy)carbonyl)amino))-3-isopropyl-2-oxo-1-piperidinyl)-3-cyclohexylpropanoyl}amino}propylboronic acid;
- 25 (1*R*)-1-{{{3-(((tert-butoxycarbonyl)amino))-3-isopropyl-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid;
- (1*R*)-1-{{{(3-amino-3-isopropyl-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid hydrochloride;
- 30

(1*R*)-1-{{{3-isopropyl-3-((methoxycarbonyl)amino)-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid;

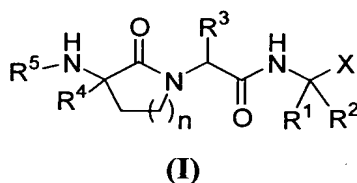
5 (1*R*)-1-{{{3-(benzoylamino)-3-isopropyl-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid;

(1*R*)-1-{{{3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid; and

10 (1*R*)-1-{{{3-isopropyl-3-{{{3-methylphenyl)sulfonyl}amino}-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid;

or a pharmaceutically acceptable salt form thereof.

15 8. A method for inhibiting proteasome which comprises contacting a mammal in need thereof with a therapeutically effective amount of a compound of Formula I:



or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

the lactam ring of Formula (I) is substituted with 0-2 R^b;

25

X is selected from the group:

B(OH)₂, BY¹Y², and C(=O)C(=O)NHR^{1a};

Y¹ and Y² are independently selected from:

30

a) -OH,

- b) -F,
- c) -NR¹⁸R¹⁹,
- d) C₁-C₈ alkoxy, or

when taken together, Y¹ and Y² form:

- 5 e) a cyclic boron ester comprising from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;
- f) a cyclic boron amide comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O; or
- 10 g) a cyclic boron amide-ester comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R¹ is selected from the group:

- C₁₋₁₀ alkyl substituted with 0-3 R^a;
- C₂₋₁₀ alkenyl substituted with 0-3 R^a;
- 15 C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
- C₃₋₆ cycloalkyl substituted with 0-3 R^a;

R^{1a} is selected from the group:

- C₁₋₁₀ alkyl substituted with 0-3 R^a;
- 20 C₂₋₁₀ alkenyl substituted with 0-3 R^a;
- C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
- C₃₋₆ cycloalkyl substituted with 0-3 R^a;

R^a is selected at each occurrence from the group:

- 25 C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH, -S-C₁₋₆ alkyl;
- phenyl substituted with 0-3 R^b;
- naphthyl substituted with 0-3 R^b;
- O-(CH₂)_q-phenyl substituted with 0-3 R^b;
- 30 -O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:

O, S, and N, and substituted with 0-3 R^b;

5 R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,
OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

10

alternatively, R¹ and R² combine to form a C₃₋₅ cycloalkyl group;

R³ is selected from the group:

C₁₋₆ alkyl substituted with 0-2 R^a;

15

C₂₋₆ alkenyl substituted with 0-2 R^a;

C₂₋₆ alkynyl substituted with 0-2 R^a;

-(CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;

-(CH₂)_q-phenyl substituted with 0-2 R^a;

-(CH₂)_q-naphthyl substituted with 0-2 R^a; and

20

-(CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4

heteroatoms selected from the group: O, S, and N, and substituted with
0-2 R^a;

R⁴ is selected from the group:

25

H;

C₁₋₆ alkyl substituted with 0-3 R^b;

phenyl substituted with 0-3 R^b;

benzyl substituted with 0-3 R^b; and

phenethyl substituted with 0-3 R^b;

30

R⁵ is H or Q-R^{5a};

Q is 0, 1, 2, or 3 amino acids;

5 R^{5a} is selected from the group:

-S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆ alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

10 C₁₋₆ alkyl substituted with 0-3 R^c;

phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms

15 selected from the group: O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;

20 benzyl substituted with 0-3 R^c; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms

selected from the group: O, S, and N, substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

25 C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,
NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

H and CH₃;

30

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

R⁸ is selected from the group:

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

5

R¹⁸ and R¹⁹ at each occurrence are independently selected from H, C₁₋₄ alkyl, aryl(C₁₋₄ alkyl)-, and C₃₋₇ cycloalkyl;

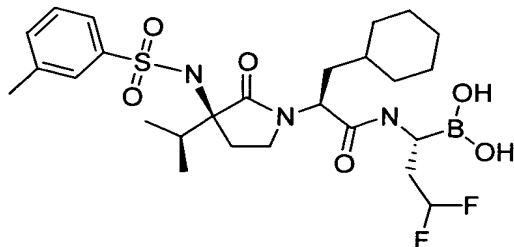
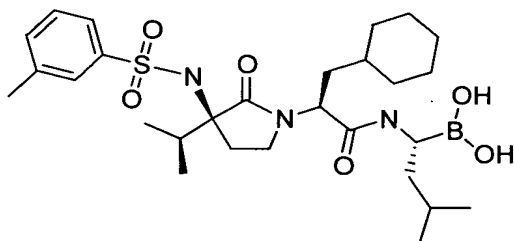
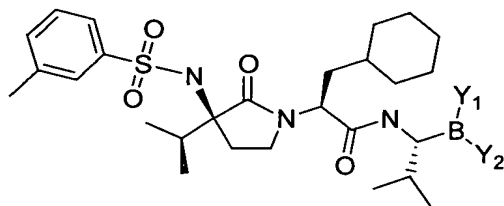
n is selected from the group:

10 1, 2, and 3; and

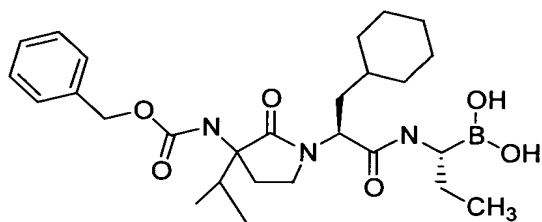
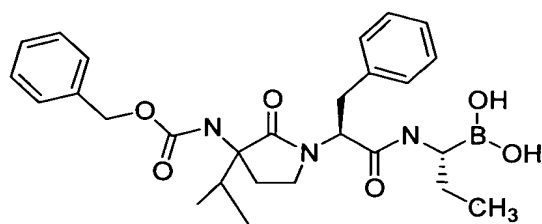
q is 0, 1, or 2.

9. The method of claim 8 wherein said compound is one of the following:

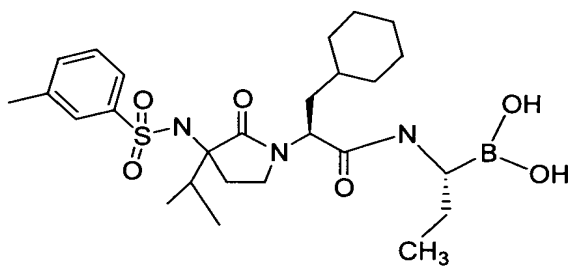
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10. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier.

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